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CLAIMS

1. A method for increasing the concentration of an HIV protease inhibitor in the brain of a patient, said method comprising administering to an HIV infected patient an amount of a 10,11-methanodibenzosuberane of formula (I):

$$\begin{bmatrix} R_1 & R_2 \\ & & \\ &$$

wherein: A is -CH₂CH₂-; -CH₂CHR^aCH₂- where R^a is H, OH or lower acyloxy; or -CH₂CHR^bCHR^cCH₂- where one of R^b or R^c is H, OH, or lower acyloxy, and the other is H;

R1 is H, F, Cl, or 3r;

R2 is H, F, Cl, or Br; and

R³ is heteroaryl or phenyl optionally substituted with F, Cl, Br, CF₃, CN, NO₂, or OCHF₂; or a pharmaceutically acceptable salt thereof; and

- co-administering to the patient a therapeutically effective amount of the protease inhibitor.
- 2. The method of claim 1 wherein the patient is a male and the concentration of the HIV protease inhibitor is also increased in the patient's testes.
- 3. The method of claim 1 wherein the protease inhibitor is selected from the group of nelfinavir, indinavir, saquinavir, ritonavir, and amprenavir.
- 4. The method of claim 3 wherein the protease inhibitor is nelfinavir.

- 5. The method of claim 1 wherein R^1 and R^2 are F, A is ${}^{-}CH_2CHR^4CH_2$ -, and R^3 is optionally substituted quinolyl.
 - 6. The method of claim 5 wherein R^a is OH and R³ is quinol-5-yl.
 - 7. The method of claim 1 wherein the methanodibenzosuberane of
- 5 formula (I) is a compound of formula (II):

F F OH

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8. A method of treating a patient having an HIV-1 infection comprising:

administering to the patient a therapeutically effective amount of a protease inhibitor, and

co-administering to the patient an amount of a compound represented

25 by formula (I):

wherein: A is $-CH_2CH_2$ -; $-CH_2CHR^aCH_2$ - where R^a is H, OH or lower acyloxy; or $-CH_2CHR^bCHR^cCH_2$ - where one of R^b or R^c is H, OH, or lower

15 acyloxy, and the other is H;

R1 is H, F, Cl, or Br;

R² is H, F, Cl, or Br; and

 R^3 is heteroaryl or phenyl optionally substituted with F, Cl, Br, CF₃, CN, NO₂, or OCHF₂; or a pharmaceutically acceptable salt thereof;

- 20 in an amount sufficient to increase brain levels of the protease inhibitor.
 - 9. The method of claim 8 wherein R¹ and R² are F, A is -CH₂CHR^aCH₂-, and R³ is optionally substituted quinolyl.
 - 10. The method of claim 9 wherein R^a is OH and R³ is quinol-5-yl.
- 25 11. The method of claim 8 wherein the amount of the compound of formula (I) is sufficient to increase the brain levels of the protease inhibitor without significantly increasing the concentration of the protease inhibitor in the patient's blood.
- 12. The method of claim 8, wherein the amount of the compound is also sufficient to increase concentrations of the protease inhibitor in the patient's testes.

13. A pharmaceutical composition comprising an antiviral protease inhibitor;

a 10,11-methanodibenzosuberane of formula (I):

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wherein: A is -CH₂CH₂-; -CH₂CHR^aCH₂- where R^a is H, OH or lower acyloxy; or -CH₂CHR^bCHR^cCH₂- where one of R^b or R^c is H, OH, or lower acyloxy, and the other is H;

R3

R¹ is H, F, Cl, or Br;

I

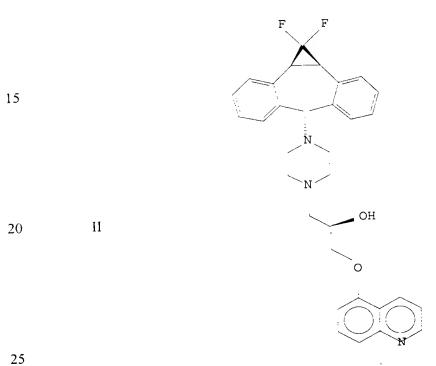
20 R² is H, F, Cl, or Br; and

 R^3 is heteroaryl or phenyl optionally substituted with F, Cl, Br, CF₃, CN, NO₂, or OCHF₂; or a pharmaceutically acceptable salt thereof;

and a pharmaceutically acceptable carrier therefor.

- 14. The composition of claim 13 wherein the
- 25 methanodibenzosuberane of formula (I) is present in an amount effective to increase brain levels of the protease inhibitor.
 - 15. The composition of claim 14 wherein the methanodibenzosuberane of formula (I) is present in an amount effective to increase brain levels of the protease inhibitor without significantly increasing plasma levels of the protease inhibitor.

- 16. The composition of claim 13 wherein the protease inhibitor is selected from the group consisting of nelfinavir, indinavir, saquinavir, ritonavir, or amprenavir.
 - 17. The composition of claim 16 wherein the protease inhibitor is
- 5 nelfinavir.
- 18. The composition of claim 13 wherein R¹ and R² are F.
- 19. The composition of claim 13 wherein A is -CH₂CHR^aCH₂-.
- 20. The composition of claim 13 wherein R3 is a optionally substituted quinolyl.
- 10 21. The composition of claim 13 wherein the 10,11-methanodibenzosuberane is the compound of formula (II):



22. The composition of claim 13 wherein the methanodibenzosuberane comprises about 0.005 to 95% of the composition.

23. Use of a 10,11-methanodibenzosuberane of formula (I):

R: R²

N

A

R3

I

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wherein: A is -CH₂CH₂-; -CH₂CHR^aCH₂- where R^a is H, OH or lower acyloxy; or -CH₂CHR^bCHR^cCH₂- where one of R^b or R^c is H, OH, or lower acyloxy, and the other is H;

R1 is H, F, C1, or Br;

R² is H, F, Cl, or Br, and

R³ is heteroaryl or phenyl optionally substituted with F, Cl, Br, CF₃,

20 CN, NO₂, or OCHF₂; or a pharmaceutically acceptable salt thereof;

for the manufacture of a medicament for the treatment of HIV in a patient undergoing treatment with an HIV protease inhibitor.

- 24. The use of claim 23 for increasing the concentration of the protease inhibitor in the brain of a patient undergoing treatment with an HIV protease inhibitor.
- 25. The use of claim 24 for increasing the concentration of the protease inhibitor in the patient's testes.
- 26. The use of any one of claims 23-25 for the manufacture of a medicament wherein the protease inhibitor is selected from the group of nelfinavir,
- 30 indinavir, saquinavir, ritonavir, and amprenavir.

- 27. The use of any one of claims 23-26 for the manufacture of a medicament wherein R¹ and R² are F, A is -CH₂CHR^aCH₂-, and R³ is optionally substituted quinolyl.
- 28. The use of claim 27 for the manufacture of a medicament wherein R^a is OH and R³ is quinol-5-yl.
 - 29. The use of claim 23 for the manufacture of a medicament for increasing brain levels of the protease inhibitor without significantly increasing plasma levels of the protease inhibitor.
- 30. Use of an HIV protease inhibitor for the manufacture of a medicament for the treatment of HIV wherein the concentration of HIV protease inhibitor in the brain is increased by co-administration with a 10,11-methanodibenzosuberane of formula (I):

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wherein: A is -CH₂CH₂-; -CH₂CHR^aCH₂- where R^a is H, OH or lower acyloxy; or -CH₂CHR^bCHR^cCH₂- where one of R^b or R^c is H, OH, or lower acyloxy, and the other is H;

R¹ is H, F, Cl, or Br;

R2 is H, F, Cl, or Br; and

R³ is heteroaryl or phenyl optionally substituted with F, Cl, Br, CF₃, CN, NO₂, or OCHF₂; or a pharmaceutically acceptable salt thereof.

- 31. The use of claim 30 wherein the concentration of the protease inhibitor in the patient's testes is also increased.
- 32. The use of any one of claims 30-31 wherein the protease inhibitor is selected from the group of nelfinavir, indinavir, saquinavir, ritonavir, and amprenavir.
 - 33. The use of claim 30 wherein the protease inhibitor is nelfinavir.
- 34. The use of any one of claims 30-33 wherein R¹ and R² are F, A is -CH₂CHR^aCH₂-, and R³ is optionally substituted quinolyl.
 - 35. The use of claim 34 wherein Ra is OH and R3 is quinol-5-yl.
- 10 36. The use of claim 30 wherein the brain levels of the protease inhibitor are increased without significantly increasing plasma levels of the protease inhibitor.